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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,131	10/11/2005	Maria-Jesus Blanco-Pillado	X-14441	7160

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EXAMINER	
CHANG, CELIA C	
ART UNIT	**PAPER NUMBER**
1625	

NOTIFICATION DATE	DELIVERY MODE
06/28/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,131	BLANCO-PILLADO ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application is a 371 of PCT/US04/09823. The continuation information has not been incorporated in the specification. To gain priority benefit, the continuation information must be incorporated in the specification.

2. A preliminary amendment was filed on Oct. 11, 2005. Claims 8, 10-13, and 16-28 have been canceled. Claims 1-7, 9, 14-15 are pending.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Pruecher et. al. CA 122L265361; Gaster et al. CA 130:13850; Eriksson et al. or CA 137:247696.

See RN 162402-52-0 anticipates compounds when Q is O, X is CR^{4c}; R^2, R^3, R^{4a}, R^{4b}, R^{4c}, R^5, R^6 are H and R^1 is alkyl/methyl.

See RN 215949-87-4 anticipates compounds when Q is O, X is CR^{4c}; R^3, R^{4b}, R^{4c}, R^5, R^6 are H and R^1 and R^2 are alkyl/methyl, R^{4a} is halo/iodo.

See RN 459819-36-4 anticipates compounds which is an acid addition salt of compounds when Q is O, X is CR^{4c}; R^2, R^3, R^{4a}, R^{4b}, R^{4c}, R^5, R^6 are H and R^1 is alkyl/methyl

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5 and 9 are rejected under 35 U.S.C. 102 (a), (b) or (e) as being anticipated by Chen CA 137:216945 or the issued US 7,105,682 (col. Col. 146, #74); or Askew et al. CA 140:16647 or the issued US 6,878,714 (col. 287 #533).

See RN 454481-41-5 anticipates compounds when Q is O, X is CR^{4c}; R^2, R^3, R^{4a}, R^{4c}, R^5, R^6 are H, R^{4b} is three fluoro substituted alkyl, and R^1 is substituted heterocylcle.

See RN 453561-92-7 anticipates compounds when Q is O, X is CR^{4c}; R^2, R^3, R^{4a}, R^{4c}, R^5, R^6 are H, R^{4b} is three fluoro substituted alkyl, and R^1 is substituted heterocylcle.

5. Claims 1-7, 9, 14-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), where the Supreme Court looked to whether the experimentation needed to practice an invention was undue or unreasonable. *Id.* An invention must be described so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". The analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *Id.* at 740, *Id.* at 1407. The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

The analysis is applied to the instant case.

Nature of invention

The claimed invention is compounds having structure of formula I for the use in treating the CNS disorder or migraine.

The state of the art and predictability

Compounds for CNS activity is a highly unpredictable field of endeavor. Ordinarily, compounds which can be used in treating CNS disorder, such as migraine, is well recognized in the art that such compound must have in vivo activity, i.e crossing the blood brain barrier as to reach the target organ (see LY344864 having in vivo activity, Phebus et al. CA 128:18603).

The amount of guidance and working examples

The specification provided compounds and their in vitro activity in isolated $5HT_{1F}$ receptor binding without any information as to the in vivo crossing of the blood and brain barrier or any correlation between the in vitro data to the in vivo data (see Wainscott et al. or Cohen et al. CA 131:266942), the specification lacks sufficient guidelines as to how to use the compounds or how to operate the method of treating/preventing migraine.

6. Claim 14-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as well as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention; or the subject matter was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The scope of claims 14-15 includes "prevention" of migraine. Medically preventing any pathological condition must provide description and enabling teaching in identifying such population which preventions is applicable; dosage and toxicity for effectively ward off symptom or disease; and absolutely no incidence of symptom or disease when the preventive measure is taken. No description in the specification as to who are the candidates that constitutes de novo prevention, what dosage without toxicity for how long so that zero incidence was obtained. Absent of such critical description and enablement, the specification failed to provide descriptive and enabling support for the claimed scope of "prevention" migraine.

Please note that a maintenance dose after diagnosis of a pathology to prevent future symptom is considered maintenance treatment and encompassed by the scope of *treatment.*

7. Claims 1-7, 9, 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the allowed claims of copending Application No. 10/569,109 in view of King.

Determination of the scope and content of the prior art (MPEP §2141.01)

The allowed claims are drawn to similar compounds of formula I, their composition and method of treating migraine.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the allowed claims is that instead of Q is O or S, the allowed claims have the Q moiety being NH. King taught that bioisosteric replacement is conventional medicinal chemical approach to locate compounds with similar potency but with different selectivity, toxicity or metabolic stability (see p.207).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of the compounds of the instant claims and the conventional bioisosteric replacement suggestion for finding better lead compound for formulation, would be motivated to modify the Q is O or S compounds with an bio-isosteric alternative NH with the expectation that such replacement would maintain potency and utility. Absent of unexpected result, such conventional suggested modification is routine endeavor around the lead compounds (see King p.208).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

The copending allowed claims, although had a later filing date, to prevent possible harassment by multiple assignees, common ownership through the enforcing of both set of claims by terminal disclaimer should be filed.

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Jun. 14, 2007

Celia Chang
Primary Examiner
Art Unit 1625